

Heterocyclic Thiones and Their Analogs in Reactions of 1,3-Dipolar Addition: V.* Reactions of 2,3,3-Triphenyl-1-thioxophthalimidine with Nitrile Imines

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Abstract—2,3,3-Triphenyl-1-thioxophthalimidine reacted with nitrile imines along the pattern of [3+2]-cycloaddition affording 2,3,3,3',5'-pentasubstituted benzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazoles). The reaction is regioselective and involves the exocyclic C=S bond.

We formerly demonstrated [1–4] that thioketones showed a high dipolarophile activity in the reactions of 1,3-dipolar cycloaddition. In the present study we continued to investigate the behavior of cyclic thioketones in 1,3-dipolar cycloaddition by an example of 2,3,3-triphenyl-1-thioxophthalimidine.

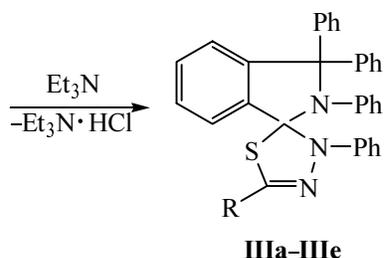
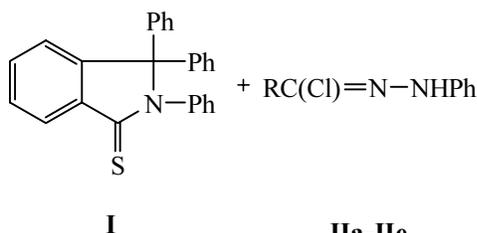
Nitrile imines were generated *in situ* by treating with triethylamine appropriate hydrazoneyl chlorides **IIa–IIe**. The reaction of 1,3-dipolar cycloaddition was carried out in boiling benzene applying equimolar quantities of 2,3,3-triphenyl-1-thioxophthalimidine (**I**) and hydrazoneyl chloride. The reaction progress was monitored by TLC. As in the cases previously studied the reaction occurred

regioselectively involving the exocyclic C=S bond following the mechanism of [3+2]-cycloaddition to yield 2,3,3,3',5'-pentasubstituted benzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazoles) **IIIa–IIIe**.

This reaction scheme is confirmed by the lack in the IR spectra of compounds obtained of the absorption band belonging to the C=S bond in the region 1260–1270 cm⁻¹ and by appearance of absorption bands at 1593–1596 and 1317–1364 cm⁻¹ corresponding to the stretching vibrations of the C=N and C–N bonds of the thiadiazole ring. In the spectra of compounds **IIIb–IIIe** the absorption bands of the stretching vibrations belonging to C=O group of substituents attached to the position 5' of thiadiazoles are observed in the region 1634–1703 cm⁻¹, and in the spectrum of compound **IIIb** the absorption bands of a nitro group appear at 1544, 1342 cm⁻¹.

The UV absorption spectra of the isolated compounds are characterized by a strong absorption maximum in the UV region (~220 nm, lg ε 4.4–4.5) (in the spectra of compounds **IIIb** and **IIIe** a shoulder additionally appears on the absorption curve and a maximum at 264 and 253 nm respectively). Less strong absorption bands are also observed in the visible region. The position on the longwave maximum in the spectra depends on the character of the substituent in the position 5' of the thiadiazole ring. A red shift of this band is observed in the series of compounds **IIIe** ≈ **IIIa** < **IIIc** < **IIIe** < **IIIb** but with a maximal change in the Δλ value 75 vs. 64 nm.

The ¹H NMR spectra of benzopyrrolidinespirothiadiazoles **IIIa–IIIe** contain the signals characteristic



R = Ph (**a**), C₆H₄NO₂-*p* (**b**), CH₃C(O) (**c**), PhC(O) (**d**), C₂H₅OC(O) (**e**).

For communication IV, see [1].

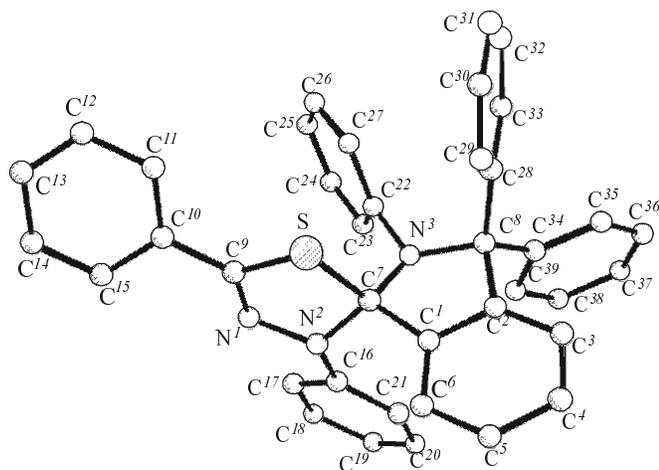
of the substituents at the carbon and nitrogen of nitrile imine, and also the signals from the aromatic protons of the benzene rings.

In the ^{13}C NMR spectra of compounds obtained the signals from the spiro carbons appeared in the region 109–119 ppm. Signals from the carbon in the position 5' of the thiadiazole ring are observed in the range 142–144 ppm. The other spectral parameters are also consistent with the assumed structure of compounds obtained.

The formation of benzopyrrolidinespirothiadiazoles **IIIa–IIIe** was also confirmed by mass spectrometry. The corresponding mass spectra contained both molecular ion peaks and peaks from fragment ions.

The structure of 2,3,3,3',5'-pentaphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (**IIIa**) was proved by X-ray diffraction analysis (see figure).

The fused benzophthalimidine system is virtually planar. The maximum deviation of atoms from the plane in the benzene ring fused to the heterocycle amounts to 0.0543 Å. The deviation of N^3 atom from the plane in the heterocycle $\text{N}^3\text{C}^1\text{C}^2\text{C}^7\text{C}^8$ is -0.131 Å, the deviation of the N^3 with respect to the plane $\text{C}^1\text{C}^2\text{C}^7\text{C}^8$ is 0.181 Å. The angle between two components of the fused system is 4.3° . (In all descriptions of results obtained by X-ray diffraction analysis the numbering of atoms is the same as on the figure). The thiadiazole ring formed as a result of the reaction is not planar, the average deviation of the atoms from the plane $\text{SN}^1\text{N}^2\text{C}^7\text{C}^9$ reaches 0.117 Å, and this ring is orthogonal to the initial system (the angle



Structure of the molecule of 2,3,3,3',5'-pentaphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (**IIIa**) according to X-ray diffraction analysis. Hydrogen atoms are not shown.

Bond lengths d (Å) and bond angles ω (deg) in the molecule of 2,3,3,3',5'-pentaphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (**IIIa**)

Bond	d	Bond	d
S–C ⁷	1.877(5)	S–C ⁹	1.753(6)
N ¹ –N ²	1.386(6)	N ¹ –C ⁹	1.287(7)
N ² –C ⁷	1.490(6)	N ² –C ¹⁶	1.426(8)
N ³ –C ⁷	1.436(6)	N ³ –C ⁸	1.497(6)
N ³ –C ²²	1.445(8)	C ¹ –C ²	1.367(7)
C ¹ –C ⁶	1.395(7)	C ¹ –C ⁷	1.503(7)
C ² –C ³	1.381(7)	C ² –C ⁸	1.528(7)
C ³ –C ⁴	1.388(8)	C ⁴ –C ⁵	1.398(9)
C ⁵ –C ⁶	1.391(8)	C ⁸ –C ²⁸	1.529(8)
C ⁸ –C ³⁴	1.547(8)	C ⁹ –C ¹⁰	1.473(8)
Angle	ω	Angle	ω
C ⁷ SC ⁹	89.7(3)	N ² N ¹ C ⁹	112.4(4)
N ¹ N ² C ⁷	115.4(4)	N ¹ N ² C ¹⁶	114.7(4)
C ⁷ N ² C ¹⁶	121.4(4)	C ⁷ N ³ C ⁸	112.1(4)
C ⁷ N ³ C ²²	118.5(4)	C ⁸ N ³ C ²²	122.5(4)
C ² C ¹ C ⁶	121.3(5)	C ² C ¹ C ⁷	110.6(4)
C ⁶ C ¹ C ⁷	128.0(5)	C ¹ C ² C ³	121.4(5)
C ¹ C ² C ⁸	110.5(4)	C ³ C ² C ⁸	128.0(4)
C ² C ³ C ⁴	117.9(5)	C ³ C ⁴ C ⁵	121.4(5)
C ⁴ C ⁵ C ⁶	119.9(5)	C ¹ C ⁶ C ⁵	118.1(5)
SC ⁷ N ²	99.7(3)	SC ⁷ N ³	117.1(3)
N ² C ⁷ N ³	113.7(4)	SC ⁷ C ¹	107.7(3)
N ² C ⁷ C ¹	116.9(4)	N ³ C ⁷ C ¹	102.3(4)
N ³ C ⁸ C ²	99.8(3)	N ³ C ⁸ C ²⁸	112.1(4)
C ² C ⁸ C ²⁸	109.0(4)	N ³ C ⁸ C ³⁴	110.7(4)
C ² C ⁸ C ³⁴	111.2(4)	C ²⁸ C ⁸ C ³⁴	113.2(4)
SC ⁹ N ¹	115.4(4)	SC ⁹ C ¹⁰	121.2(4)
N ¹ C ⁹ C ¹⁰	123.3(5)	C ⁹ C ¹⁰ C ¹¹	121.2(5)
C ⁹ C ¹⁰ C ¹⁵	118.9(6)	N ² C ¹⁶ C ¹⁷	119.1(6)
N ² C ¹⁶ C ²¹	121.6(7)	N ³ C ²² C ²³	118.1(6)
N ³ C ²² C ²⁷	121.7(7)	C ⁸ C ²⁸ C ²⁹	120.0(6)
C ⁸ C ²⁸ C ³³	121.1(6)	C ²⁹ C ²⁸ C ³³	118.7(7)
C ²⁸ C ²⁹ C ³⁰	120.6(7)	C ²⁹ C ³⁰ C ³¹	120.4(8)
C ³⁰ C ³¹ C ³²	119.2(8)	C ³¹ C ³² C ³³	121.1(7)
C ²⁸ C ³³ C ³²	119.9(7)	C ⁸ C ³⁴ C ³⁵	120.0(6)
C ⁸ C ³⁴ C ³⁹	120.7(5)		

between the planes $\text{SN}^1\text{N}^2\text{C}^7\text{C}^9$ and $\text{N}^3\text{C}^1\text{C}^2\text{C}^7\text{C}^8$ equals to 89.1°). The bond lengths and bond angles are given in the table.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord 75IR from solutions of compounds **IIIa–IIIe** in CHCl_3 (cell thickness 0.97 mm). Electronic spectra were

taken on spectrometer Specord UV-Vis (l 1 cm) from solutions in acetonitrile. NMR spectra were registered on spectrometer Bruker AM-500 (500 MHz for ^1H NMR, 125 MHz for ^{13}C), ^1H NMR spectra from 5% solutions of compounds in $\text{DMSO}-d_6$, and ^{13}C spectra from 5% solutions in CDCl_3 , internal reference HMDS. Mass spectra were obtained on a MKh-1321 instrument, vaporizer temperature 120°C , ionizing chamber temperature 200°C , ionizing voltage 70 V.

X-ray diffraction study of a single crystal of 2,3,3,3',5'-pentaphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (**IIIa**) was performed on an automatic diffractometer Syntex P-1 (MoK_α -radiation, Nb-filter $\theta/2\theta$ -scanning, $2\theta \leq 45^\circ$). Monoclinic crystals: $\text{C}_{39}\text{H}_{29}\text{N}_3\text{S}$. a 10.426(2), b 15.402(3), c 18.913 (3) Å, β 97.19 (2°), V 3013.2(1.8) Å³; space group $P2_1/c$, Z 4, d_{calc} 1.260 g/cm³. The structure was solved by the direct method [1960 reflections with $I > 2\sigma(I)$] in full-matrix approximation, anisotropic for atoms C, N, O, S, and isotropic for hydrogen atoms, till R 0.045, R_w 0.050 (no correction for extinction was done). The calculations were performed along software SHELXTL on a minicomputer NOVA-3. A perspective drawing of the molecule is represented on the figure, the bond lengths and bond angles are given in the table. The crystallographic coordinates of nonhydrogen and hydrogen atoms and their equivalent thermal factors are available from the authors.

Preparation procedure for 2,3,3-triphenyl-1-thioxophthalimidine. A mixture of 1.05 g of 2,3,3-triphenylphthalimidine [5] and 0.75 g of P_4S_{10} in 15 ml of anhydrous *o*-xylene was boiled for 30 min, the hot solution was filtered, the solvent was removed, and the residue was recrystallized from ethanol. Yield 0.66 g (60%), mp $223\text{--}225^\circ\text{C}$.

Nitrile imines were generated *in situ* by treating with the triethylamine the corresponding hydrazoneyl chlorides **Ia–Ie** [6].

General procedure for reaction between 1-thioxophthalimidine and C-aryl(acetyl, benzoyl, ethoxycarbonyl)-*N*-phenylnitrile imines **Ia–Ie.** To a solution of 2 mmol of 1-thioxophthalimidine in 30 ml of anhydrous toluene was added in succession 2 mmol of an appropriate hydrazoneyl chloride **II** and 4 mmol of triethylamine. The reaction mixture was boiled for 1 h. On cooling the precipitate of triethylamine hydrochloride was filtered off, the filtrate was evaporated under reduced pressure, and the residue was crystallized by grinding with ether. The products obtained were recrystallized from acetonitrile.

2,3,3,3',5'-Pentaphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (IIIa**).** Yield 90%, mp $223\text{--}224^\circ\text{C}$. IR spectrum, ν , cm^{-1} : 1596 (C=N), 1336, 1326 (C–N). Electronic spectrum (CH_2Cl_2), λ_{max} , nm ($\lg \epsilon$): 349 (4.00). ^1H NMR spectrum, δ , ppm: 6.53–7.78 m (29 H, H_{arom}). ^{13}C NMR spectrum, δ , ppm: 79.834 (C^3), 109.765 ($\text{C}^{1(2)}$), 119.486, 121.872, 124.987, 125.041, 126.160, 126.712, 127.211, 127.467, 127.575, 127.778, 128.196, 128.344, 128.452, 128.613, 129.085, 129.786, 130.204, 132.173, 132.253, 139.157, 139.723, 140.869, 142.878, 143.080, 143.822 (C_{arom}), 144.376 (C^5). Mass spectrum, m/z (I_{rel} , %): 571 (2) [$\text{C}_{39}\text{H}_{29}\text{N}_3\text{S}]^+$, 462 (30) [$\text{C}_{33}\text{H}_{24}\text{N}_3$]⁺, 194 (55) [$\text{C}_{13}\text{H}_{10}\text{N}_2$]⁺, 121 (30) [$\text{C}_7\text{H}_5\text{S}$]⁺, 91 (100) [$\text{C}_6\text{H}_5\text{N}$]⁺, 77 (40) [C_6H_5]⁺. Found, %: C 81.62; H 5.25; S 5.56. $\text{C}_{39}\text{H}_{29}\text{N}_3\text{S}$. Calculated, %: C 81.92; H 5.12; S 5.61.

5'-(*p*-Nitrophenyl)-2,3,3,3'-tetraphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (IIIb**).** Yield 89%, mp $227\text{--}228^\circ\text{C}$. IR spectrum, ν , cm^{-1} : 1593 (C=N), 1333, 1317 (C–N), 1544, 1342 (NO_2). Electronic spectrum (CH_3CN), λ_{max} , nm ($\lg \epsilon$): 420 (4.09). ^1H NMR spectrum, δ , ppm: 6.52–8.17 m (28 H, H_{arom}). ^{13}C NMR spectrum, δ , ppm: 79.807 (C^3), 119.279 ($\text{C}^{1(2)}$), 122.862, 123.919, 124.618, 124.904, 126.317, 126.802, 127.431, 127.787, 128.389, 128.544, 128.844, 129.258, 130.999, 138.180 (C_{arom}), 142.448 (C^5). Mass spectrum, m/z (I_{rel} , %): 507 (40) [$\text{C}_{33}\text{H}_{23}\text{N}_4\text{O}_2$]⁺, 377 (90) [$\text{C}_{26}\text{H}_{19}\text{NS}$]⁺, 376 (100) [$\text{C}_{26}\text{H}_{18}\text{NS}$]⁺, 300 (65) [$\text{C}_{20}\text{H}_{13}\text{NS}$]⁺, 239 (35) [$\text{C}_{13}\text{H}_9\text{N}_3\text{O}_2$]⁺, 91 (95) [$\text{C}_6\text{H}_5\text{N}$]⁺, 77 (95) [C_6H_5]⁺. Found, %: C 75.65; H 4.73; S 5.00. $\text{C}_{39}\text{H}_{28}\text{N}_4\text{O}_2\text{S}$. Calculated, %: C 75.94; H 4.58; S 5.20.

5'-Acetyl-2,3,3,3'-tetraphenylbenzo[*c*]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (IIIc**).** Yield 83%, mp $188\text{--}189^\circ\text{C}$. IR spectrum, ν , cm^{-1} : 1598 (C=N), 1364, 1314 (C–N), 1680 (C=O). Electronic spectrum (CH_2Cl_2), λ_{max} , nm ($\lg \epsilon$): 365 (4.07). ^1H NMR spectrum, δ , ppm: 2.21 s (3H, CH_3), 6.46–7.78 m (24H, H_{arom}). ^{13}C NMR spectrum, δ , ppm: 25.001 (CH_3), 80.482 (C^3), 111.079 ($\text{C}^{1(2)}$), 120.743, 123.574, 124.006, 125.125, 125.179, 126.716, 127.242, 127.323, 127.457, 127.619, 127.781, 127.848, 128.266, 128.442, 128.536, 128.711, 129.021, 129.601, 129.790, 130.127, 132.473, 132.635, 138.392, 138.540, 139.120, 141.857, 142.410, 142.572, 142.626 (C_{arom}), 144.432 (C^5), 191.218 (C=O). Mass spectrum, m/z (I_{rel} , %): 537 (20) [$\text{C}_{35}\text{H}_{27}\text{N}_3\text{OS}$]⁺, 428 (20) [$\text{C}_{29}\text{H}_{19}\text{N}_3\text{O}$]⁺, 377 (22) [$\text{C}_{26}\text{H}_{19}\text{NS}$]⁺, 376 (32) [$\text{C}_{26}\text{H}_{18}\text{NS}$]⁺, 77 (100) [C_6H_5]⁺. Found, %: C 77.90; H 5.20; S 5.86. $\text{C}_{35}\text{H}_{27}\text{N}_3\text{OS}$. Calculated, %: C 76.15; H 5.16; S 5.65.

5'-Benzoyl-2,3,3,3'-tetraphenylbenzo[c]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (IIIId). Yield 81%, mp 140–141.5°C. IR spectrum, ν , cm^{-1} : 1595 (C=N), 1369 (C–N), 1312 (C–N), 1634 (C=O). Electronic spectrum (CH_3CN), λ_{max} , nm ($\log \epsilon$): 386 (3.96). ^1H NMR spectrum, δ , ppm: 6.54–7.88 (m) (29H, H_{arom}). ^{13}C NMR spectrum, δ , ppm: 80.054 (C^3), 109.420 ($\text{C}^{1(2)}$), 120.255, 124.452, 124.938, 127.094, 127.522, 127.793, 127.951, 128.164, 128.322, 128.479, 128.621, 128.750, 129.007, 129.335, 130.691, 130.934, 132.847, 135.588, 137.872, 138.301, 140.999, 141.270, 141.684 (C_{arom}), 144.154 (C^5), 184.370 (C=O). Mass spectrum, m/z (I_{rel} , %): 599 (30) [$\text{C}_{40}\text{H}_{29}\text{N}_3\text{OS}$] $^+$, 490 (50) [$\text{C}_{34}\text{H}_{24}\text{N}_3\text{O}$] $^+$, 377 (20) [$\text{C}_{26}\text{H}_{19}\text{NS}$] $^+$, 376 (25) [$\text{C}_{26}\text{H}_{18}\text{NS}$] $^+$, 105 (95) [$\text{C}_6\text{H}_5\text{N}_2$], 77 (100) [C_6H_5] $^+$. Found, %: C 79.87; H 5.02; S 4.98. $\text{C}_{40}\text{H}_{29}\text{N}_3\text{OS}$. Calculated, %: C 80.10; H 4.88; S 5.34.

5'-Ethoxycarbonyl-2,3,3,3'-tetraphenylbenzo[c]pyrrolidine-1-spiro-2'-(2',3'-dihydro-1',3',4'-thiadiazole) (IIIe). Yield 84%, mp 196–197°C. IR spectrum, ν , cm^{-1} : 1596 (C=N), 1342, 1319 (C–N), 1703 (C=O), 1139, 1071 (C–O). Electronic spectrum (CH_3CN), λ_{max} , nm ($\log \epsilon$): 345 (3.92). ^1H NMR spectrum, δ , ppm: 1.18 t (3H, CH_3 , J 7 Hz), 4.17 q (2H, CH_2 , J 7 Hz), 6.48–7.83 m (24H, H_{arom}). ^{13}C NMR spectrum, δ , ppm: 13.927

(CH_3), 61.452 (CH_2), 79.911 (C^3), 110.591 ($\text{C}^{1(2)}$), 120.527, 124.253, 124.738, 124.910, 126.651, 127.508, 127.721, 127.907, 128.322, 128.536, 128.978, 130.177, 130.606, 131.748, 138.386, 141.641 (C_{arom}), 143.883 (C^5), 159.458 (C=O). Mass spectrum, m/z (I_{rel} , %): 567 (10) [$\text{C}_{36}\text{H}_{29}\text{N}_3\text{O}_2\text{S}$] $^+$, 458 (50) [$\text{C}_{30}\text{H}_{24}\text{N}_3\text{O}_2$] $^+$, 377 (20) [$\text{C}_{26}\text{H}_{19}\text{NS}$] $^+$, 376 (30) [$\text{C}_{26}\text{H}_{18}\text{NS}$] $^+$, 300 (23) [$\text{C}_{20}\text{H}_{13}\text{NS}$] $^+$, 190 (10) [$\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2$] $^+$, 91 (28) [$\text{C}_6\text{H}_5\text{N}$] $^+$, 77 (100) [C_6H_5] $^+$. Found, %: C 75.94; H 5.23; S 5.36. $\text{C}_{36}\text{H}_{29}\text{N}_3\text{O}_2\text{S}$. Calculated, %: C 76.15; H 5.16; S 5.65.

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